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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
KETTER, J

ART UNIT	PAPER NUMBER
1805	4

DATE MAILED: 01/27/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 11/25/91 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire THREE month(s); _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|-----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input checked="" type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input checked="" type="checkbox"/> Notice of Informal Patent Application, Form PTO-152 |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-32 are pending in the application.
Of the above, claims 1-9 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 10-32 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☒ not been received
☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

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Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 10-32, drawn to a method of cloning, classified in Class 435, subclass 172.3 and 91.

II. Claims 1-9, drawn to a receptor, classified in Class 530, subclass 350(+).

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (M.P.E.P. § 806.05(f)). In the instant case the product as claimed can be made by a materially different process, such as cleavage of pre-existing antibody, or through the use of cloning and expression systems different than those employed.

Because these inventions are distinct for the reasons given above and have acquired separate statuses in the art as shown by their different classifications, restriction for examination purposes as indicated is proper.

During a telephone conversation with Arthur Crawford on 16 January 1992, a provisional election was made with traverse to prosecute the invention of Group I, claims 10-32. Affirmation of

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this election must be made by applicant in responding to this Office action. Claims 1-9 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 11, 14-18, and 27 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mullis et al. (A). Mullis et al. disclose the PCR technique, including the use of a mixture of primers for ambiguous target sequences (column 8, first full

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paragraph). Applicants have disclosed a series of process steps which broadly claim PCR.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 10, 11, 14-19, 22, 27, 29, 30, and 32 are rejected under 35 U.S.C. § 103 as being unpatentable over Mullis et al.

(A). Instant claims are drawn to a process of making amplified DNA. As such, instant claims employ the methods disclosed by Mullis et al. merely using different starting materials, i.e., primers, DNA, and vectors. Claimed novelty in the starting materials and/or final product does not lend patentability to an art-known process of making. It would have been obvious to one of ordinary skill in the art to have employed the PCR methods

taught by Mullis et al. to amplify any known target DNA molecule. The motivation to have done so would have been that PCR is and was known to be a generally applicable technique to a broad range of DNA molecules, as is indicated in, e.g., Mullis et al. at column 2, fourth full paragraph.

Claims 1-22 and 26-32 are rejected under 35 U.S.C. § 103 as being unpatentable over Skerra et al. (R) in view of either Mullis et al. (A) or Herzog et al. (B), and in view of Kabat et al. (S). Skerra et al. teach the cloning and expression in E. coli of DNA segments encoding Fv fragments. Mullis et al. disclose the PCR technique to amplify and clone DNA segments, including the use of a mixture of primers for ambiguous target sequences (column 8, first full paragraph). Herzog et al. disclose the use of PCR to amplify and clone DNA segments, including the use of a mixture of primers to amplify related but different DNA sequences. Kabat et al. disclose DNA sequences of heavy and light immunoglobulin chains. It would have been obvious to one of ordinary skill in the art to have modified the teachings of Skerra et al. by using mixed primer PCR, as taught by either Mullis et al. or Herzog et al., based upon the DNA sequences taught by Kabat et al. The motivation to have employed PCR would have been that PCR is and was known to be a generally applicable technique to a broad range of DNA molecules, as is indicated in, e.g., Mullis et al. at column 2, fourth full

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paragraph. The motivation to have used mixed primers would have been that Kabat et al. disclose the degree of variability in the DNAs which encode immunoglobulin heavy and light chain variable regions.

Claims 23-25 are rejected under 35 U.S.C. § 103 as being unpatentable over Skerra et al. in view of either Mullis et al. or Herzog et al., and in view of Kabat et al. as applied to claims 1-22 and 26-32 above, and further in view of Schoemaker et al. (C). Schoemaker et al. teach the expression of heterochain antibodies. It would have been obvious to one of ordinary skill in the art to have practiced the invention of claims 1-22 and 26-32 with the modification of expressing the Ig fragments together as heterochain antibodies. The motivation to have done so would have come from Schoemaker et al., column 2, fourth full paragraph, where it is disclosed that heterochain antibodies can be superior to the "parental" antibodies from which the chains were derived.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

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The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-30 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 27, step "(g)" would introduce nicks into said DNA, making cloning of said DNA difficult or impossible, as said DNA duplex would be less thermally stable, and also as the host (E. coli) would likely degrade nicked DNA before replication, as is well-known in the art. Applicants have neither described nor enabled the avoidance of this problem when nicking said DNA molecules.

With respect to claims 27-30, only one cycle of PCR (polymerase chain reaction) is claimed, prior to the cloning

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step. Clearly, this would lead only to a two-fold amplification of the target DNA, which would be insufficient for cloning said DNA as disclosed.

With respect to claim 28, the method, as claimed, omits a denaturation step, such as "(b)" in the independent claim 27, and would thus not operate.

It would appear that the claims have not been drafted in such a way as to either be: enabled by the specification, i.e., the invention as claimed could not be practiced according to the teachings of the specification, as the claimed series of steps do not appear to be operable; or to particularly point out and distinctly claim the invention disclosed in the specification, i.e., the claims do not describe the disclosed invention.

Claims 1-32 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the PCR primers disclosed in the specification, and therefore to the mammalian immunoglobulin genes amplified using said primers. See M.P.E.P. §§ 706.03(n) and 706.03(z). A large amount of experimentation of an uncertain nature would be required to select other primer sequences which would produce functional antibody fragments as claimed. Such would be undue

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experimentation.

Claims 10-13, 15, 16, 21, 22, 24, 25, 27-29, and 32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 10, the method of instant claim is not a "method of cloning", but is instead a method of amplifying. The use of the term cloning renders the claim confusing.

With respect to claims 10 and 27, "hybridise" should be "hybridize". With further respect to claims 10 and 27, process step "(a)" in each claim adds nothing to the respective claim, as it would be necessary to "provide", i.e., "have" a certain starting material in order to perform a process thereupon.

With respect to claim 11, "plurality of times" is indefinite.

With respect to claims 12 and 13, instant claims are drawn to "[t]he method...which is used to". Such a claim structure is not statutory, as it is essentially a method of using a method of

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making. It is unclear as to what is actually being claimed.

With respect to claim 13, instant claim is dependent on two other claims simultaneously, i.e., not in the alternative. As such, instant claim is non-statutory in structure.

With respect to claim 15, "closely related" is vague and/or indefinite, as it does not specify a quantitative degree of similarity.

With respect to claim 16, "species specific general" is vague.

With respect to claim 21, "sequence which is annealed" is vague, in that it is a primer which is annealing.

With respect to claim 22, it is unclear what "expressed alone" means.

With respect to claim 24, the term "one or more" is vague in that it does not define an upper limit to the number of said domains claimed.

With respect to claim 25, it is not clear which noun is meant to be the antecedent of "it".

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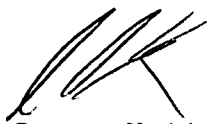
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With respect to claim 28, it is not clear what or which "recombinant plasmids" are intended, rendering instant claim unclear.

With respect to claim 29, it is unclear what the antecedent basis of "fragments" is.

With respect to claim 32, "sequence which anneals" is vague, in that it is a primer which anneals.

Any inquiry concerning this or any other communication from the examiner should be directed to James Ketter, who may be contacted at (703) 308-0408.



James Ketter
January 27, 1992



RICHARD A. SCHWARTZ
SUPERVISORY PATENT EXAMINER
ART UNIT 185



**UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY DOCKET NO./TITLE
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DATE MAILED:

NOTICE OF INFORMAL APPLICATION

(Attachment to Office Action)

This application does not conform with the rules governing applications for the reason(s) checked below. The period within which to correct these requirements and avoid abandonment is set in the accompanying Office action.

A. A new oath or declaration, identifying this application by the application number and filing date is required. The oath or declaration does not comply with 37 CFR 1.63 in that it:

1. ☐ does not identify the city and state or foreign country of residence of each inventor.
2. ☐ does not identify the citizenship of each inventor.
3. ☐ does not state whether the inventor is a sole or joint inventor.
4. ☐ does not state that the person making the oath or declaration:
 - a. ☐ has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.
 - b. ☐ believes the named inventor or inventors to be the original and first inventor or inventors of the subject matter which is claimed and for which a patent is sought.
 - c. ☐ acknowledges the duty to disclose information which is material to the examination of the application in accordance with 37 CFR 1.56(a).
5. ☐ does not identify the foreign application for patent or inventor's certificate on which priority is claimed pursuant to 37 CFR 1.55, and any foreign application having a filing date before that of the application on which priority is claimed, by specifying the application serial number, country, day, month, and year of its filing.
6. ☐ does not state that the person making the oath or declaration acknowledges the duty to disclose material information as defined in 37 CFR 1.56(a) which occurred between the filing date of the prior application and filing date of the continuation-in-part application which discloses and claims subject matter in addition to that disclosed in the prior application (37 CFR 1.63(d)).
7. ☐ does not include the date of execution.
8. ☒ does not use permanent ink, or its equivalent in quality, as required under 37 CFR 1.52(a).
9. ☐ contains non-initialed alterations (See 37 CFR 1.52(c)).

10. ☒ Other: PARENT APPLICATION S/N 07/580,374 WAS NOT COMPLETE AT TIME THIS APPLICATION WAS FILED. THEREFORE A SIGNED OATH OR DECLARATION IS REQUIRED. SEE 37 CFR 1.60.

B. Applicant is required to provide:

1. ☐ A statement signed by applicant giving his or her complete name. A full name must include at least one given name without abbreviation as required by 37 CFR 1.41(a).
2. ☐ Proof of authority of the legal representative under 37 CFR 1.44.
3. ☐ An abstract in compliance with 37 CFR 1.72(b).
4. ☐ A statement signed by applicant giving his or her complete post office address (37 CFR 1.33(a)).
5. ☐ A copy of the specification written, typed, or printed in permanent ink, or its equivalent in quality as required by 37 CFR 1.52(a).
6. ☐ Other:

ATTACHED TO PAPER NO. 4.